



NOTES

PNS DEMYELINATING DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Progressive peripheral nervous system (PNS) disorders; destruction of myelin, disruption of motor, sensory function

TYPES

Charcot-Marie-Tooth disease

- Genetic mutations → defective myelin sheath, impaired neuronal mitochondrial function

Guillain-Barré syndrome

- Acute triggering event (e.g. infection) → aberrant autoimmune response → myelin sheath destruction

COMPLICATIONS

Charcot-Marie-Tooth disease

- Muscle atrophy, impaired ambulation, foot irregularities

Guillain-Barré syndrome

- Respiratory failure, cardiac arrhythmias, quadriplegia

SIGNS & SYMPTOMS

- ↓/absent deep tendon reflexes, paresthesia, muscle weakness, ↓ touch sensation

DIAGNOSIS

DIAGNOSTIC IMAGING

Gadolinium-enhanced MRI

- Guillain-Barré
 - Intrathecal spinal nerve root thickening

LAB RESULTS

- Guillain-Barré
 - Albuminocytologic dissociation in cerebrospinal fluid (CSF)

OTHER DIAGNOSTICS

- Electromyography (EMG), nerve conduction studies (NCS)
 - ↓/blocked nerve conduction velocity
- History, physical examination

TREATMENT

MEDICATIONS

- Guillain-Barré
 - Intravenous immunoglobulin (IVIg)

SURGERY

- Charcot-Marie-Tooth
 - Correction of severe skeletal irregularities

OTHER INTERVENTIONS

- Charcot-Marie-Tooth
 - Genetic testing, orthotics, physical/occupational therapy
- Guillain-Barré
 - Plasmapheresis; supportive care (e.g. respiratory/hemodynamic support)
- Pain management
 - Acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentin, carbamazepine

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CHARCOT–MARIE–TOOTH DISEASE

osms.it/Charcot-Marie-Tooth

PATHOLOGY & CAUSES

- Group of hereditary, progressive neurological disorders; disruption of PNS processes, impaired sensory/motor function
- Genetic mutations → defective structure, function of proteins in myelin sheath/neuron's axon
- **Classification:** Types I–VII; Type X (X-linked)
 - Subtypes based on associated genes and phenotypes

TYPES

Charcot–Marie–Tooth I (CMT1)

- Demyelinating form
 - Caused by mutations in *PMP22*, *MPZ* genes (encode for myelin sheath proteins) → ↓ nerve conduction velocity
 - Autosomal dominant/sporadic inheritance

CMT2

- Axonal form
 - Caused by mutations in *MFN2* gene (encodes for mitofusin-2 protein in neuronal mitochondria) → neuronal death
 - Autosomal dominant/recessive inheritance

RISK FACTORS

- Inheritance of defective gene(s)

COMPLICATIONS

- Muscle atrophy, loss of ambulation; deafness, intellectual disability, optic neuropathy, feeding difficulties, hip dysplasia

SIGNS & SYMPTOMS

- Onset in first to third decade of life, depending on type
- Progressive distal muscle weakness; atrophy of hands, feet
- Distal sensory loss, paresthesias, loss of proprioception
- ↓ deep tendon reflexes, areflexia
- Foot irregularities
 - Foot drop, high arches (pes cavus), hammer toes, flail foot, cavovarus foot
- Unsteady gait, toe-walking

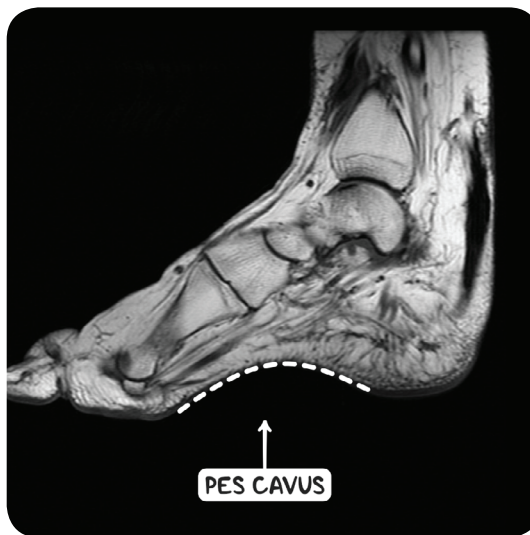


Figure 87.1 An MRI scan of the foot of an individual with Charcot-Marie-Tooth disease. There is wasting of the plantar muscles and prominent pes cavus as well as a hammer irregularity of the great toe.

DIAGNOSIS

OTHER DIAGNOSTICS

- NCS, EMG
 - ↓ nerve conduction velocity
- History, physical examination (e.g. age of onset)
- Genetic testing

TREATMENT

MEDICATIONS

- Pain management
 - Acetaminophen, NSAIDs, gabapentin, carbamazepine

SURGERY

- Correction of severe skeletal irregularities

OTHER INTERVENTIONS

- Physical/occupational therapy
 - Strengthening, range of motion, balance, maintenance of mobility, activities of daily living
- Orthotics

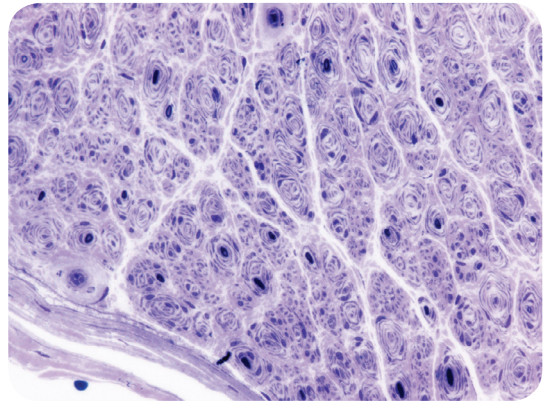


Figure 87.2 A section of a peripheral nerve from an individual with Charcot–Marie–Tooth disease.

GUILLAIN–BARRÉ SYNDROME

osms.it/guillain-barre-syndrome

PATHOLOGY & CAUSES

- Acute, progressive demyelinating PNS disease; sensory, motor, cognitive deficits
- AKA acute inflammatory demyelinating polyneuropathy
- Abnormal autoimmune response
 - Myelin autoantigen picked up by antigen-presenting cells (e.g. dendritic) → antigen presented to helper T-cells → production of cytokines → activation of B-cells and macrophages → B-cells make antibodies, mark autoantigens; macrophages use antibody markers to attack myelin sheath on peripheral neurons → ↓/blocked nerve conduction velocity; axonal degeneration

Variants

- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
- Miller–Fisher syndrome
 - Affects cranial nerves (CN) III, IV, VI
- Acute motor axonal neuropathy (AMAN)
- Acute sensorimotor axonal neuropathy (AMSAN)

CAUSES

- Molecular mimicry between microbe, nerve antigens
 - Most commonly associated with *Campylobacter jejuni*, *Mycoplasma pneumoniae*, cytomegalovirus, Epstein–Barr, influenza A, Zika, HIV

RISK FACTORS

- Acute infection
- ↑ age
- More common in individuals who are biologically male

COMPLICATIONS

- Acute
 - Ileus, urinary retention, cardiac arrhythmias, pneumonia, respiratory failure, quadriplegia
- Long-term
 - Chronic fatigue, chronic pain, relapses

SIGNS & SYMPTOMS

- Variable presentation, depending on affected nerve
- Bilateral, flaccid, ascending weakness of limbs, peaking ≤ four weeks
- ↓ deep tendon reflexes, areflexia, touch sensation
- Paresthesia
- Diaphragmatic weakness → breathing difficulties (e.g. hypoventilation, requires mechanical ventilation)
- Autonomic involvement
 - Hypertension/hypotension/postural hypotension, bradycardia
- CN involvement
 - Blurred vision, dysarthria, abnormal pupillary response to light

DIAGNOSIS

DIAGNOSTIC IMAGING

Gadolinium-enhanced MRI (spine)

- T1-weighted images
 - Thickening of intrathecal spinal nerve roots

LAB RESULTS

- CSF
 - Albuminocytologic dissociation (high levels of protein without increase in cell counts)
- Serum immunoglobulin G (IgG) antibodies to ganglioside Q1b (GQ1b)
 - Miller–Fisher

OTHER DIAGNOSTICS

- EMG, NCS
 - ↓/blocked nerve conduction velocity
- History, physical examination

TREATMENT

MEDICATIONS

- IVIG
- Gabapentin/carbamazepine
 - Pain management

OTHER INTERVENTIONS

- Plasmapheresis
- Respiratory/hemodynamic support